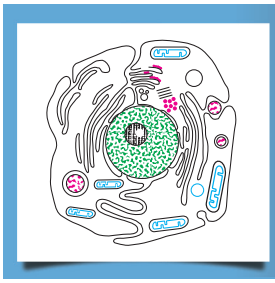
1 Biomolecules and the Cell



The cell speaks

"I am the unit of biological activity;
Organized into subcellular organelles;
Assigned to each are specific duties;
Thus, I truly represent life!"

Competencies as per the NMC – CBME curriculum, 2024

Competency No.	Competency
BC1.1 (+ Chapter 33)	Describe the molecular and functional organization of a cell and its subcellular components and composition and functions of Biological membranes.

The general aspects of biomolecules, the structure and organization of cell and cellular components are described in this chapter. The composition and functions of ***biological membranes*** are discussed in ***Chapter 33***.

The living matter is composed of mainly six elements – ***carbon***, ***hydrogen***, ***oxygen***, ***nitrogen***, ***phosphorus*** and ***sulfur***. These elements together constitute about 90% of the dry weight of the human body. Several other functionally important elements are also found in the cells. These include: Ca, K, Na, Cl, Mg, Fe, Cu, Co, I, Zn, F, Mo and Se.

Carbon—a unique element of life

Carbon is the most predominant and versatile element of life. It possesses a unique property to ***form infinite number of compounds***. This is attributed to the ability of carbon to form stable covalent bonds and C—C chains of unlimited length. It is estimated that about ***90% of compounds*** found in living system invariably ***contain carbon***.

Chemical molecules of life

Life is composed of lifeless chemical molecules. A single cell of the bacterium, *Escherichia coli* contains about 6,000 different organic compounds. It is believed that man may contain about 100,000 different types of molecules, although only a few of them have been characterized.

Complex biomolecules

The organic compounds such as ***amino acids***, ***nucleotides*** and ***monosaccharides*** serve as the ***monomeric units*** or building blocks of complex biomolecules – ***proteins***, ***nucleic acids*** (DNA and RNA) and ***polysaccharides***, respectively. The important biomolecules (macromolecules) with their respective building blocks and major functions are

Table 1.1 The major complex biomolecules of cells

Biomolecule	Building blocks (repeating units)	Major functions
1. **Protein**	Amino acids	Fundamental basis of structure and function of cell (static and dynamic functions).
2. **Deoxyribonucleic acid (DNA)**	Deoxyribonucleotides	Repository of hereditary information.
3. **Ribonucleic acid (RNA)**	Ribonucleotides	Essentially required for protein biosynthesis.
4. **Polysaccharide (glycogen)**	Monosaccharides (glucose)	Storage form of energy to meet short term demands.
5. **Lipid**	Fatty acids, glycerol	Storage form of energy to meet long term demands; structural components of membranes.

given in ***Table 1.1***. As regards lipids, it may be noted that they are not biopolymers in a strict sense, but majority of them contain fatty acids.

Structural hierarchy of an organism

The ***macromolecules*** (proteins, lipids, nucleic acids and polysaccharides) form ***supramolecular assemblies*** (e.g. membranes) which in turn organize into organelles, cells, tissues, organs and finally the whole organism.

Chemical composition of man

The chemical composition of a normal man, weighing 65 kg, is given in ***Table 1.2***. Water is ***the solvent of life*** and contributes to more than 60% of the body weight. This is followed by protein (mostly in muscle) and lipid (mostly in adipose tissue). The carbohydrate content is rather low which is in the form of glycogen.

THE CELL

The cell is the structural and functional unit of life. It may be also regarded as the ***basic unit of biological activity.***

Table 1.2 Chemical composition of a normal man (weight 65 kg)

Constituent	Percent (%)	Weight (kg)
Water	61.6	40
Protein	17.0	11
Lipid	13.8	9
Carbohydrate	1.5	1
Minerals	6.1	4

Prokaryotic and eukaryotic cells

The cells of the living kingdom may be divided into two categories:

1. **Prokaryotes** (*Greek* : pro – before; karyon – nucleus) ***lack a well defined nucleus*** and possess relatively simple structure. These include the various bacteria.

2. **Eukaryotes** (*Greek* : eu – true; karyon – nucleus) possess a ***well defined nucleus*** and are more complex in their structure and function. The higher organisms (animals and plants) are composed of eukaryotic cells.

A comparison of the characteristics between prokaryotes and eukaryotes is listed in ***Table 1.3***.

EUKARYOTIC CELL

The human body is composed of about 10^{14} cells. There are about 250 types of specialized cells in the human body e.g. erythrocytes, nerve cells, muscle cells, β cells of pancreas. An eukaryotic cell is generally 10 to 100 µm in diameter. A diagrammatic representation of a typical rat liver cell is depicted in ***Fig.1.1***.

The plant cell differs from an animal cell by possessing a rigid cell wall (mostly composed of cellulose) and chloroplasts. The latter are the sites of photosynthesis.

The cell consists of well defined subcellular organelles, enveloped by a plasma membrane. By differential centrifugation of tissue homogenate, it is possible to isolate each cellular organelle in a relatively pure form (***Refer Chapter 41***). The distribution of major enzymes and metabolic pathways in different cellular organelles is given in the chapter on enzymes (***Refer Table 6.7***). The

Origins of Important Words

Arthritis *(Greek)* arthron–joint; itis–inflammation
Biochemistry *(Greek)* bios–life; chymos–juice
Biology *(Greek)* bios–life; logos–discourse
Cathepsin *(Greek)* to digest
Chromosome *(Greek)* chroma–colour; soma–body
Cristae *(Latin)* crests
Cytology *(Greek)* kytos–cell; logos–discourse
Cytoplasm *(Greek)* kytos–cell; plassein–to mould
Eukaryotes *(Greek)* eu-true; karyon–nucleus
Mitochondria *(Greek)* mitos–thread; chondros-granule
Progeria *(Greek)* prematurely old
Prokaryotes *(Greek)* pro–before; karyon–nucleus
Syndrome (*Greek*) syn–together; dramein–to run

Common Confusables

Prokaryotes; eukaryotes – Prokaryotes are the cells that lack a well defined nucleus; eukaryotes possess a well-defined nucleus.

subcellular organelles are briefly described in the following pages.

Nucleus

Nucleus is the ***largest cellular organelle***, surrounded by a double membrane nuclear envelope. The outer membrane is continuous with the membranes of endoplasmic reticulum. At certain intervals, the two nuclear membranes have nuclear pores with a diameter of about 90 nm. These pores permit the free passage of the products synthesized in the nucleus into the surrounding cytoplasm.

Table 1.3 Comparison between prokaryotic and eukaryotic cells

Characteristic	Prokaryotic cell	Eukaryotic cell
1. **Size**	Small (generally 1-10 μm)	Large (generally 10-100 μm)
2. **Cell membrane**	Cell is enveloped by a rigid cell wall	Cell is enveloped by a flexible plasma membrane
3. **Sub-cellular organelles**	Absent	Distinct organelles are found (e.g. mitochondria, nucleus, lysosomes)
4. **Nucleus**	Not well defined; DNA is found as nucleoid, histones are absent	Nucleus is well defined, surrounded by a membrane; DNA is associated with histones
5. **Cell division**	Usually fission and no mitosis	Mitosis

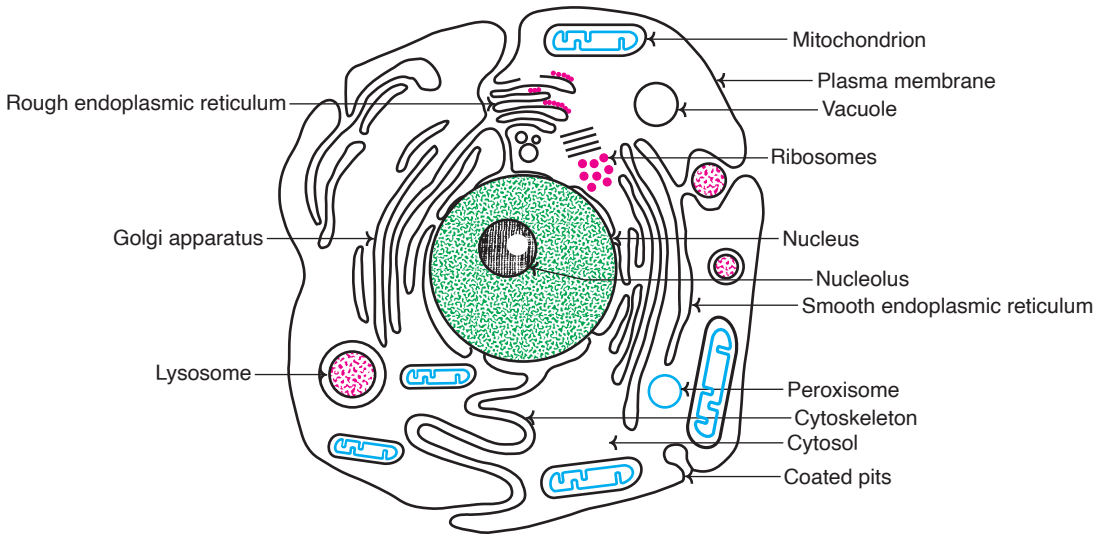


Fig. 1.1 : *Diagrammatic representation of a rat liver cell.*

Nucleus contains ***DNA***, the repository of genetic information. Eukaryotic DNA is associated with basic protein (histones) in the ratio of 1 : 1, to form ***nucleosomes***. An assembly of nucleosomes constitutes ***chromatin*** fibres of chromosomes (*Greek*: chroma – colour; soma – body). Thus, a single human chromosome is composed of about a million nucleosomes. The number of chromosomes is a characteristic feature of the species. ***Humans have 46 chromosomes***, compactly packed in the nucleus.

The nucleus of the eukaryotic cell contains a dense body known as ***nucleolus***. It is rich in RNA, particularly the ribosomal RNA which enters the cytosol through nuclear pores.

The ground material of the nucleus is often referred to as ***nucleoplasm***. It is rich in enzymes such as DNA polymerases and RNA polymerases.

Hutchinson-Gilford progeria syndrome (HGPS) is a rare condition of ***aging beginning at birth*** (incidence 1 in 5 million births). HGPS occurs as a result of distortion of nuclear envelope due to accumulation of abnormal protein namely ***lamin A***.

Mitochondria

The mitochondria (*Greek*: mitos – thread; chondros – granule) are the centres for the cellular respiration and energy metabolism. They are regarded as the ***power houses of the cell*** with variable size and shape. Mitochondria are rod-like or filamentous bodies, usually with dimensions of 1.0 × 3 µm. About 2,000 mitochondria, occupying about $\frac{1}{5}$th of the total cell volume, are present in a typical cell.

The mitochondria are composed of a double membrane system (***Refer Fig.11.5***). The outer membrane is smooth and completely envelops the organelle. The inner membrane is folded to form ***cristae*** (*Latin* – crests) which occupy a larger surface area. The internal chamber of mitochondria is referred to as ***matrix*** or ***mitosol***.

The components of ***electron transport chain*** and ***oxidative phosphorylation*** (flavoprotein, cytochromes b, c_1, c, a and a_3 and coupling factors) are buried in the inner mitochondrial membrane. The matrix contains several enzymes concerned with the energy metabolism of carbohydrates, lipids and amino acids (e.g., ***citric acid cycle, β-oxidation***). The matrix enzymes also participate in the synthesis of heme and urea. Mitochondria are the ***principal producers of ATP*** in the aerobic cells. ATP, the energy currency, generated in mitochondria is exported to all parts of the cell to provide energy for the cellular work.

Progeria

The ***mitochondrial*** matrix contains a circular double stranded ***DNA*** (***mtDNA***), RNA and ribosomes. Thus, the mitochondria are equipped with an ***independent protein synthesizing machinery***. It is estimated that about 10% of the mitochondrial proteins are produced in the mitochondria.

The structure and functions of mitochondria closely ***resemble prokaryotic cells***. It is hypothesized that mitochondria have evolved from aerobic bacteria. Further, it is believed that during evolution, the aerobic bacteria developed a symbiotic relationship with primordial anaerobic eukaryotic cells that ultimately led to the arrival of aerobic eukaryotes.

Endoplasmic reticulum

The ***network of membrane enclosed spaces*** that extends throughout the cytoplasm constitutes endoplasmic reticulum (ER). Some of these thread-like structures extend from the nuclear pores to the plasma membrane.

A large portion of the ER is studded with ribosomes to give a granular appearance which is referred to as ***rough endoplasmic reticulum***. ***Ribosomes are the factories of protein biosynthesis***. During the process of cell fractionation, rough ER is disrupted to form small vesicles known as ***microsomes***. It may be noted that microsomes as such do not occur in the cell.

The smooth endoplasmic reticulum does not contain ribosomes. It is involved in the synthesis of lipids (triacylglycerols, phospholipids, sterols) and metabolism of drugs, besides supplying Ca^{2+} for the cellular functions.

Medical Concepts

- Leakage of lysosomal enzymes into the cell degrades several functional macromolecules and this may lead to certain disorders (e.g. arthritis).
- Defect of a cytoskeleton protein, namely spectrin in RBC results in hereditary spherocytosis. This causes breakdown of RBC, leading to anemia.

Curiosity Corner

Mitochondria possess a circular and independent DNA with genes and machinery to produce proteins. Can the mitochondria synthesize all the proteins needed for their structure and functions?

Ans. ***No.*** Mitochondria can produce only 13 proteins which are a part of complexes in electron transport chain. A vast majority of proteins (around 1500) are encoded by nuclear DNA.

Golgi apparatus

Eukaryotic cells contain a unique cluster of ***membrane vesicles*** known as ***dictyosomes*** which, in turn, constitute Golgi apparatus (or Golgi complex). The newly synthesized proteins are handed over to the Golgi apparatus which catalyse the addition of carbohydrates, lipids or sulfate moieties to the proteins. These chemical modifications are necessary for the transport of proteins across the plasma membrane.

Certain proteins and enzymes are enclosed in membrane vesicles of Golgi apparatus and secreted from the cell after the appropriate signals. The ***digestive enzymes of pancreas*** are produced in this fashion.

Golgi apparatus are also involved in the ***membrane synthesis***, particularly for the formation of intracellular organelles (e.g. peroxisomes, lysosomes).

Lysosomes

Lysosomes are spherical vesicles enveloped by a single membrane. Lysosomes are regarded as the ***digestive tracts of the cell***, since they are actively involved in digestion of cellular substances – namely proteins, lipids, carbohydrates and nucleic acids. Lysosomal enzymes are categorized as ***hydrolases***. These include the enzymes (with substrate in brackets) – α-glucosidase (glycogen), cathepsins (proteins), lipases (lipids), ribonucleases (RNA).

The lysosomal enzymes are responsible for ***maintaining the cellular compounds in a dynamic state***, by their degradation and recycling. The degraded products leave the lysosomes, usually by diffusion, for reutilization by the cell. Sometimes, however, certain residual products, rich in lipids and proteins, collectively known as ***lipofuscin*** accumulate in the cell. Lipofuscin is the ***age pigment*** or wear and tear pigment which has been implicated in aging process. As the cell dies, the lysosomes rupture and release hydrolytic enzymes that results in post-mortem autolysis.

The digestive enzymes of cellular compounds are confined to the lysosomes in the best interest of the cell. Escape of these enzymes into cytosol will destroy the functional macromolecules of the cell and result in many complications. The occurrence of several diseases (e.g. ***arthritis***, muscle diseases, allergic disorders) has been partly attributed to the ***release of lysosomal enzymes***.

Inclusion cell (I-cell) disease is a rare condition due to the absence of certain hydrolases in lysosomes. However, these enzyme are synthesized and found in the circulation. I-cell disease is due to ***a defect in protein targetting***, as the ***enzymes cannot reach lysosomes***.

Peroxisomes

Peroxisomes, also known as ***microbodies***, are single membrane cellular organelles. They are spherical or oval in shape and contain the enzyme ***catalase***. Catalase protects the cell from the toxic effects of H_2O_2 by converting it to H_2O and O_2. Peroxisomes are also involved in the oxidation of long chain fatty acids ($> C_{18}$), and synthesis of plasmalogens and glycolipids. Plants contain ***glyoxysomes***, a specialized type of peroxisomes, which are involved in the glyoxylate pathway.

Peroxisome biogenesis disorders (PBDs), are a group of rare diseases involving the enzyme activities of peroxisomes. The biochemical abnormalities associated with PBDs include increased levels of very long chain fatty acids (C_{24} and C_{26}) and decreased concentrations of plasmalogens. The most severe form of PBDs is ***Zellweger syndrome***, a condition characterized by the absence of functional peroxisomes. The victims of this disease may die within one year after birth.

BC1.1 **Table 1.4 A summary of subcellular organelles, their major functions and associated disorders**

Feature	Major function(s)	Associated disorders
Nucleus	Controls cell activities and gene expression	Cancer, progeria, lamins-related diseases
Mitochondria	ATP production, metabolism, apoptosis.	Mitochondrial myopathy, Leber's hereditary optic neuropathy.
Endoplasmic reticulum (ER)	Protein/lipid synthesis, detoxification.	Cystic fibrosis, neurodegenerative diseases
Golgi apparatus	Protein/lipid modification and sorting.	Golgi syndrome, Tay-Sachs disease.
Lysosomes	Digestion of macromolecules and pathogens.	Tay-Sachs, Gaucher's, Pompe disease.
Peroxisomes	Fatty acid breakdown, detoxification.	Zellweger syndrome, Adrenoleukodystrophy
Ribosomes	Protein synthesis	Diamond-Blacktan anemia, Shwachman-Diamond syndrome.
Cytoskeleton	Structural support, cell shape, transport.	Ciliopathies, muscular dystrophy.
Plasma membrane	Substance regulation, communication.	Cystic fibrosis, hereditary spherocytosis.
Vacuoles	Storage, turgor pressure.	Autophagic vacuolar pathology.

Cytosol and cytoskeleton

The ***cellular matrix*** is collectively referred to as cytosol. Cytosol is basically a compartment containing several enzymes, metabolites and salts in an aqueous gel like medium. More recent studies however, indicate that the cytoplasm actually contains a complex network of protein filaments, spread throughout, that constitutes ***cytoskeleton***. The cytoplasmic filaments are of three types – ***microtubules***, actin filaments and intermediate filaments. The filaments which are polymers of proteins are responsible for the structure, shape and organization of the cell.

A summary of subcellular organelles, their major functions and associated disorders is given in ***Table 1.4.***

INTEGRATION OF CELLULAR FUNCTIONS

The eukaryotic cells perform a wide range of complex reactions/functions to maintain tissues, and for the ultimate well-being of the whole organism. For this purpose, the various intracellular processes and biochemical reactions are tightly controlled and integrated. Division of a cell into two daughter cells is good example of the orderly occurrence of an integrated series of cellular reactions.

Apoptosis is the ***programmed cell death*** or ***cell suicide***. This occurs when the cell has fulfilled its biological functions. Apoptosis may be regarded as a ***natural cell death*** and it differs from the cell death caused by injury due to radiation, anoxia etc. Programmed cell death is a highly regulated process.

SUMMARY

- *The cell is the structural and functional unit of life. The eukaryotic cell consists of well defined subcellular organelles, enveloped in a plasma membrane.*
- *The nucleus contains DNA, the repository of genetic information. DNA, in association with proteins (histones), forms nucleosomes which, in turn, make up the chromosomes.*
- *The mitochondria are the centres for energy metabolism. They are the principal producers of ATP which is exported to all parts of the cell to provide energy for cellular work.*
- *Endoplasmic reticulum (ER) is the network of membrane enclosed spaces that extends throughout the cytoplasm. ER studded with ribosomes, the factories of protein biosynthesis, is referred to as rough ER.*
- *Lysosomes are the digestive bodies of the cell, actively involved in the degradation of cellular compounds. Peroxisomes contain the enzyme catalase that protects the cell from the toxic effects of H_2O_2.*
- *The eukaryotic cells perform a wide range of complex functions in a well coordinated and integrated fashion. Apoptosis is the process of programmed cell death or cell suicide.*

Self - Assessment Exercises

1. Describe the functional organization of the cell with special reference to nucleus, mitochondria and lysosomes.

Clinical Scenario - based MCQs

(i) A 50-year old male presented with frequent fatigue and progressive muscle weakness. He showed increased activity of serum creatine kinase. Name the subcellular organ mostly likely affected, in this patient.

(a) Lysosomes (b) Golgi apparatus
(c) Ribosomes (d) Mitochondria

Multiple Choice Questions (MCQs)

1. **The most predominant chemical constituent of life**
   (A) Water (B) Protein
   (C) Lipid (D) Carbohydrate.
2. **One of the following cannot form a polymer in the living cell**
   (A) Monosaccharides (B) Amino acids
   (C) Fatty acids (D) Ribonucleotides.
3. **The mitochondrial DNA (mtDNA) is**
   (A) Circular double stranded
   (B) Circular single stranded
   (C) Linear double helix (D) None of the above.
4. **The cellular organelle regarded as the digestive tract of the cell**
   (A) Nucleus (B) Golgi appratus
   (C) Peroxisome (D) Lysosome.
5. **The cellular organelle predominantly responsible for respiration and energy metabolism**
   (A) Glyoxysomes (B) Golgi apparatus
   (C) Mitochondria (D) Nucleus.
6. **The pH of the lysosomal matrix is**
   (A) Equal to that of cytosol
   (B) More acidic than cytosol
   (C) More basic than cytosol (D) Neutral

Answers

(i) **d**; 1. (**A**) 2. (**C**) 3. (**A**) 4. (**D**) 5. (**C**) 6. (**B**).

Clinical Case Studies–Analysis, and Resoning Questions

Case Study 1.1

A child of 2 years age had delayed growth, short height, small face, hair toss. It was observed that the child was aging faster than usual.

1. **What is the provisional diagnosis?**
2. **What is the biochemical basis of this disorder?**
3. **What are the complications of this disease?**

Ans. :

1. **Hutchinson-Gilford progeria syndrome (HGPS) or simply progeria.**
2. A gene mutation is responsible for progeria. Normally, Lamin A (LMNA) gene produces protein lamin A that holds nucleus at the center of the cell and maintains the integrity of the cell. Mutation of lamin A gene results in an abnormal protein, progerin that makes cells unstable leading to premature aging.
3. Alopecia (hair loss), wrinkled skin, small face, loss of eyesight, kidney failure, athero-sclerosis, heart disease. Average life span is around 15 years.

For related clinical case study, refer 14.4

Viva/Short Questions

1. **Name the structural and functional unit of life.**
   The cell.
2. **Which element is most abundantly present in biomolecules?**
   Carbon.
3. **The hydrolase enzymes of the cell are predominantly localized in the subcellular organelle, namely**
   Lysosomes.
4. **Name the pigment that accumulates in the cells as the age advances.**
   Lipofuscin.
5. **Where are the enzymes of energy metabolism present in a prokaryotic cell?**
   Cell membrane.
6. **Name the disorder where rapid aging begins at birth**
   Hutchinson-Gilford progeria syndrome (HGPS).
7. **What do you understand by apoptosis?**
   Programmed cell death or cell suicide.